

## Alcoholism Isn't What It Used To Be

*"NIAAA's goal now and for the foreseeable future is to develop and disseminate research-based resources for each stage of the alcohol use disorder continuum, from primary prevention to disease management," according to acting NIAAA director Ken Warren, Ph.D.*

The realization dawned gradually as researchers analyzed data from NIAAA's 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). In most persons affected, alcohol dependence (commonly known as alcoholism) looks less like Nicolas Cage in *Leaving Las Vegas* than it does your party-hardy college roommate or that hard-driving colleague in the next cubicle.

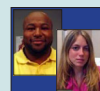
"We knew from the 1991–1992 National Longitudinal Alcohol Epidemiologic Study that alcohol dependence is most prevalent among younger adults aged 18 to 29," says Bridget Grant, Ph.D., Ph.D., chief of NIAAA's

Laboratory Epidemiology and Biometry. "However, it was not until we examined the NESARC data that we pinpointed age 22 as the mean age of alcohol dependence onset." Subsequent analysis by Ralph Hingson, Sc.D., director, Division of Epidemiology and Prevention Research, showed that nearly half of people who become alcohol dependent do so by age 21 and two-thirds by age 25.

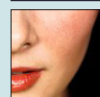
The NESARC surveyed more than 43,000 individuals representative of the U.S. adult population using questions based on criteria in the *Diagnostic and Statistical Manual of Mental Disorders*,

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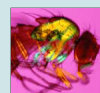
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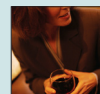
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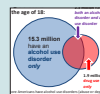
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Dr. Bridget Grant

# NIAAA

National Institute on Alcohol  
Abuse and Alcoholism

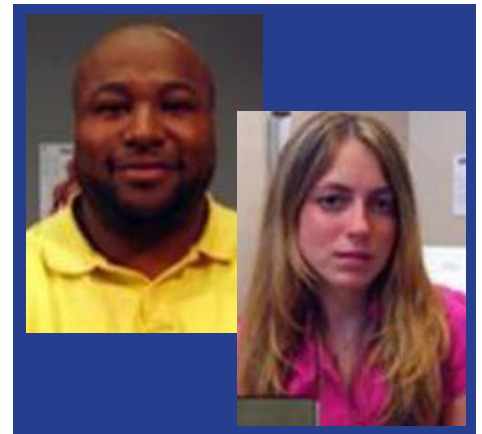
*Fourth Edition* (DSM-IV) of the American Psychiatric Association (APA). Published in 1994, DSM-IV recognizes alcohol dependence by preoccupation with drinking, impaired control over drinking, compulsive drinking, drinking despite physical or psychological problems caused or made worse by drinking, and tolerance and/or withdrawal symptoms.

Meanwhile, findings continue to accumulate to challenge past perceptions of the nature, course, and outcome of alcoholism. Among those findings:

- Many heavy drinkers do not have alcohol dependence. For example, even in people who have 5 or more drinks a day (the equivalent of a bottle of wine) the rate of developing dependence is less than 7 percent per year.
- Most persons who develop alcohol dependence have mild to moderate disorder, in which they primarily experience impaired control. For example, they

set limits and go over them or find it difficult to quit or cut down. In general, these people do not have severe alcohol-related relationship, health, vocational, or legal problems.

- About 70 percent of affected persons have a single episode of less than 4 years. The remainder experience an average of five episodes. Thus, it appears that there are two forms of alcohol dependence: time-limited, and recurrent or chronic.
- Although 22 is the average age when alcohol dependence begins, the onset varies from the mid-teens to middle age.
- Twenty years after onset of alcohol dependence, about three-fourths of individuals are in full recovery; more than half of those who have fully recovered drink at low-risk levels without symptoms of alcohol dependence.



- About 75 percent of persons who recover from alcohol dependence do so without seeking any kind of help, including specialty alcohol (rehab) programs and Alcoholics Anonymous. Only 13 percent of people with alcohol dependence ever receive specialty alcohol treatment.

"These and other recent findings turn on its head much of what we thought we knew about alcoholism," according to Mark Willenbring, M.D., director of NIAAA's Division of Treatment and Recovery Research. "As is so often true in medicine, researchers have studied the patients seen in hospitals and clinics most intensively. This can greatly skew understanding of a disorder, especially in the alcohol field, where most people neither seek nor receive treatment and those who seek it do so well into the course of

*These and other recent findings turn on its head much of what we thought we knew about alcoholism.*

disease. Longitudinal, general population studies such as the NESARC permit us to see the entire disease continuum from before onset to late-stage disease."

To Willenbring, these realizations call for a public health approach that targets at-risk drinkers and persons with mild alcohol disorder to prevent or arrest problems before they progress. NIAAA is addressing this need with tools to expand risk awareness (<http://rethinkingdrinking.niaaa.nih.gov>) and inform secondary prevention and primary care screening (<http://www.niaaa.nih.gov/guide>).

New criteria to guide clinicians in diagnosis and treatment await decisions by the DSM-V committee, expected about 2012. Both Dr. Grant and Howard Moss, M.D, associate director for clinical and translational research, represent NIAAA on that committee.

"NIAAA's goal now and for the foreseeable future is to develop and disseminate research-based resources for each stage of the alcohol use disorder continuum, from primary prevention to disease management," according to acting NIAAA director Ken Warren, Ph.D. ■

## Alcohol "Flush" Signals Increased Cancer Risk Among East Asians



*"We estimate that at least 540 million people have this alcohol-related increased risk for esophageal cancer," said first author Philip J. Brooks, Ph.D., of NIAAA's Laboratory of Neurogenetics.*

Many people of East Asian descent possess an enzyme deficiency that causes their skin to redden, or flush, when they drink alcohol. Scientists from NIAAA and Japan's Kurihama Alcohol Center now caution that heavy alcohol consumption greatly increases the risk for esophageal cancer among such individuals, who comprise about 8 percent of the world's population. Their review of recent research on this topic appeared in the March 24, 2009, issue of PLoS Medicine.

"We estimate that at least 540 million people have this alcohol-related increased risk for esophageal cancer," said first author Philip J. Brooks, Ph.D., of NIAAA's Laboratory of Neurogenetics. "Cancer of the esophagus is particularly deadly, with 5-year survival rates ranging from 12 to 31 percent throughout the world. We hope that, by raising

awareness of this important public health problem, affected individuals who drink will reduce their cancer risk by limiting their alcohol consumption."

The affected enzyme, known as aldehyde dehydrogenase 2 (ALDH2), plays an important role in alcohol metabolism. Alcohol is first metabolized into acetaldehyde, a toxic chemical that causes DNA damage and has other cancer-promoting effects. ALDH2 is the main enzyme responsible for breaking down acetaldehyde into acetate, a non-toxic metabolite.

East Asians have two main variants of the ALDH2 gene: one that produces an enzyme with normal activity, and another that results in an inactive enzyme. When individuals with the inactive variant drink alcohol, acetaldehyde accumulates in the body, resulting in facial flushing, nausea, and rapid heartbeat. For

people with two copies of the inactive variant, these symptoms are so severe that they can drink very little alcohol. However, individuals with only one copy of the inactive variant can become tolerant to the unpleasant effects of acetaldehyde, which puts them at risk for alcohol-related esophageal cancer.

A series of epidemiologic studies by Akira Yokoyama and his colleagues in Japan have shown that individuals with one copy of the inactive variant are about 6 to 10 times more likely to develop esophageal cancer than are individuals with the fully active ALDH2 enzyme who drink comparable amounts of alcohol.

Dr. Yokoyama is a co-author of the latest report.

The researchers add that many ALDH2-deficient university students may have their first experiences with heavy drinking while in college. Therefore, it is particularly important for university health professionals to be aware of the relationship between ALDH2-deficiency, facial flushing, and alcohol-related cancer risk. Informing ALDH2-deficient young people of their risk of esophageal cancer from alcohol drinking represents a valuable and cost-effective opportunity for cancer prevention.

Dr. Brooks and his colleagues said that a clinician can reliably determine whether a patient is at risk simply by asking about previous episodes of facial flushing after drinking alcohol. From this perspective, they noted, the flushing response is a clinically useful biomarker of genetic susceptibility to esophageal cancer risk from alcohol. ■

The article abstract can be found here: *The alcohol flushing response: An unrecognized risk factor for esophageal cancer from alcohol consumption.*  
<http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000050>



## Estimating Blood Alcohol Levels in Children

**D**rink for drink, the average blood alcohol concentrations (BACs) attained by children and adolescents are much higher than those seen among college students or adults, according to a new study supported by NIAAA

that appeared in the June 2009 issue of *Pediatrics*.

Using previously published health surveys and scientific reports, researchers derived total body water data and alcohol elimination rates—key variables

in the BAC equation—for individuals ranging in age from 9 to 17. With that information, researchers were able to modify the equation used for estimating BACs in adults to estimate the BACs that theoretically would result after children and adolescents consume various numbers of drinks. No alcohol was provided to children or adolescents as part of this research.

With the modified equation, researchers can better determine how to assess child or adolescent binge drinking. NIAAA defines binge drinking as a pattern of alcohol consumption that brings BAC to .08 grams percent or above, the legal limit for



driving in all 50 States. For the typical adult male, this pattern corresponds to consuming 5 or more drinks in about 2 hours (4 or more drinks for adult females). A drink is defined as an alcohol beverage that contains 0.6 fluid ounces or 14 grams of “pure” alcohol, the approximate content in a 12-ounce regular beer, 5-ounce glass of wine, or 1½ -ounce shot of 80-proof distilled spirits.

The study determined that girls aged 9 to 17 can be “legally intoxicated” after having as few as 3 drinks in a 2-hour period. Similarly, the study’s authors estimate that a BAC of .08 or higher would also result among boys aged 9 to 13 who consume 3 drinks within 2 hours.

According to the study’s author, John E. Donovan, Ph.D., the findings suggest that children may experience physical and psychological effects after drinking less than a full drink. Research has shown that the expectation of experiencing such effects increases the likelihood of starting to drink and of involvement in problem drinking in adolescence. ■

The article abstract can be found here: *Estimated blood alcohol concentrations for child and adolescent drinking and their implications for screening instruments.*

[http://www.ncbi.nlm.nih.gov/pubmed/19482748?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19482748?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)



## How **NOT** To Raise a College Binge Drinker

*Parental approval or disapproval of drinking makes a difference*

Parents who allow their children to drink alcohol in high school are not protecting their children from abusing alcohol when they leave the home for college, report researchers from the Prevention Research and Methodology Center at Pennsylvania State University. Parental disapproval of drinking, however, does seem to have a protective effect against alcohol misuse in college.

The findings, presented by the study’s author, Caitlin Abar, at the annual meeting of the Society for Prevention Research were published in the June–July 2009 issue of *Addictive Behaviors*. In this study, the researchers surveyed 290 college freshmen on their parents’ attitudes toward alcohol, as well as on the students’ drinking habits. Additionally, students answered questions about their own experiences with negative effects of alcohol, such as hangovers, drunken driving, and risky sexual behavior as a result of drinking.

Parental allowance of alcohol consumption in late high school was a significant risk factor for alcohol misuse and its consequences in college. “Specifically, it appears that the limits parents set for their teens with regard to alcohol consumption are particularly important,” note the authors. Teens who were permitted to drink at fairly high levels were more likely to drink heavily in college than their peers who were not allowed to drink, or whose parents had very low limits for what they considered acceptable drinking behavior. The findings were true for both males and females who participated in the study. ■

The article abstract can be found here: *The impact of parental modeling and permissibility on alcohol use and experienced negative drinking consequences in college.*

[http://www.ncbi.nlm.nih.gov/pubmed/19398278?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19398278?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)



# Lancet Series Examines Alcohol's Impact on Global Health

*Articles address alcohol's burden and harm reduction strategies*

*Worldwide, 6.3 percent of deaths in men and 1.1 percent of deaths in women are attributable to alcohol.*

In its June 27, 2009, issue, *The Lancet* published a series of articles on alcohol and global health, specifically addressing alcohol's burden, harm-reduction strategies, and actions to address the issue. The series features three papers covering the economic costs attributable to alcohol use and alcohol use disorders, the cost-effectiveness of policies and programs to reduce alcohol's harm, as well as a "call to action" for reducing harm from alcohol.

Jürgen Rehm, Ph.D., and colleagues analyzed World Health Organization (WHO) data and determined that, worldwide, 6.3 percent of deaths in men and 1.1 percent of deaths in women are attributable to alcohol. The researchers also found that alcohol is responsible for the

loss of 4.6 percent of disability-adjusted life years around the world, and—in middle- and high-income countries—for the loss of 1 percent of gross domestic product.

Also in the series, Peter Anderson, M.D., and co-authors review interventions that may reduce alcohol-related harm for efficacy and cost-effectiveness. They determined that proven strategies for reducing harm include: taxation, drunk-driving legislation, bans on advertising, limiting availability of alcohol, and providing help for dangerous drinking.

In their call to action, Sally Casswell, Ph.D., and Thaksaphon Thamarangsi, Ph.D., argue that alcohol-related harm has received less attention from

WHO compared with that of illicit drugs and tobacco. They suggest a legally-binding Framework Convention on Alcohol Control that would be supported by nongovernmental organizations in concert with WHO.

In addition to the articles in the series, this issue of *The Lancet* also includes a study from David Zaridze, M.D., and co-authors showing that alcohol was the cause of more than half of deaths in Russian men between 15–54 years from 1990–2001. The study of nearly 50,000 adults in three Russian cities contributes to an explanation for the life expectancy of 59 years for Russian men vs. 76 years for men in the UK. ■

The entire series, as well as editorials and commentary can be found here: *The Lancet Series on Alcohol and Global Health.*

<http://www.thelancet.com/series/alcohol-and-global-health/>



# “Happyhour” Gene Hints at New Alcohol Treatment

A class of drugs already approved as cancer treatments might also help to beat alcohol addiction. That’s the conclusion of a discovery in flies of a gene, dubbed “happyhour,” that has an important role in controlling the insects’ response to alcohol. The study was published in the May 29, 2009, edition of the journal *Cell*.

Animals with a mutant version of the gene grow increasingly resistant to alcohol’s sedative effects, the research shows. The researchers report further evidence that the gene normally does its work by blocking the so-called epidermal growth factor (EGF) pathway. That EGF

pathway is best known for its role in cancer, and drugs designed to inhibit the EGF receptor (including erlotinib and gefitinib) are FDA-approved for the treatment of non-small cell lung cancer.

Now, researchers have shown that flies and mice treated with erlotinib also grow more sensitive to alcohol. What’s more, rats given the cancer-fighting drug spontaneously consumed less alcohol that was freely available to them. Their taste for another rewarding beverage—sugar water—was unaffected.

Earlier studies have shown that fruit flies are a useful tool for unraveling the basis for

the effects of alcohol. Several genes previously identified as playing a role in fruit flies’ alcohol response hold parallel roles in mammals. In search of similar genes in the new study, the researchers screened mutant flies for those less sensitive to ethanol. That screen led them to happyhour, a gene closely related to mammalian enzymes known as the Ste20-family kinases of the GCK-1 subfamily.

Author Ulrike Heberlein, Ph.D., said they still don’t know exactly how alcohol exerts its influence on the EGFR pathway or how that leads to the telltale changes in behavior that come with alcohol intoxication. Those questions will be the subject of future investigation. Her team is also exploring other new gene candidates that turned up in the fly screens. She says that several of those appear to be tied to the EGFR pathway in different ways.

“It’s not yet clear how it all fits together,” she said. “But the fact that we’ve come, in an unbiased way, to molecules in the same pathway is telling us this is really, really important.” ■

The article abstract can be found here: *Happyhour, a Ste20 family kinase, implicates EGFR signaling in ethanol-induced behaviors.*  
[http://www.ncbi.nlm.nih.gov/pubmed/19464045?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19464045?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)

# Young, Tech-Savvy, and Drinking Too Much

*"Cyber Millennials," the Nation's tech-savvy singles and couples living in fashionable neighborhoods on the urban fringe, have the highest rate of risky levels of alcohol drinking.*



// Audience segmentation" refers to categorizing people by their behaviors, attitudes, opinions, or lifestyles. It is widely used in social-marketing efforts. A new study from NIAAA researchers uses this method to find high-risk drinkers in the U.S., leading researchers to a group dubbed the Cyber Millennials: the Nation's tech-savvy singles and couples living in fashionable neighborhoods on the urban fringe. Results were published in the August 2009 issue of *Alcoholism: Clinical & Experimental Research*.

Researchers used multiple marketing-research data sources merged with CDC's Behavioral

Risk Factor Surveillance System database. They performed a segmentation analysis of those individuals who self-reported consuming 5 or more drinks per drinking episode at least twice in the preceding 30 days.

"We identified the top-10 audience segments in the U.S. that engaged in twice-a-month, high-risk drinking," explained Howard B. Moss, M.D., associate director for Clinical and Translational Research at NIAAA. "Five of these audience segments were made up of young adults, and five were middle-aged individuals. The young adult segment we called the 'Cyber Millennials,' with the highest rate of risky levels of alcohol drinking, represented well-educated, ethnically mixed, technologically sophisticated individuals who live in urban fringe areas on the West Coast and Middle Atlantic regions."

One of the surprising things about this group, added Dr. Moss, was that it is one of the most health-conscious segments of American society. "They have a lower-than-average smoking

rate, they go to the gym, they consume organic produce, yet they binge drink at a level that is clearly detrimental to their well-being."

"Clinicians tend to be more blasé with younger, healthier patients, and might not even ask them about their level of alcohol consumption or screen them for alcohol problems," said Dr. Moss. "Since half of our top-10 high-risk drinking segments are young adults, clinicians might want to 'ratchet up' their index of suspicion when these individuals present clinically. Asking about drinking behavior, giving advice, or conducting a formal brief intervention might save lives in the short-term, and reduce the risk of later development of alcohol-related organ damage or alcohol dependence." ■

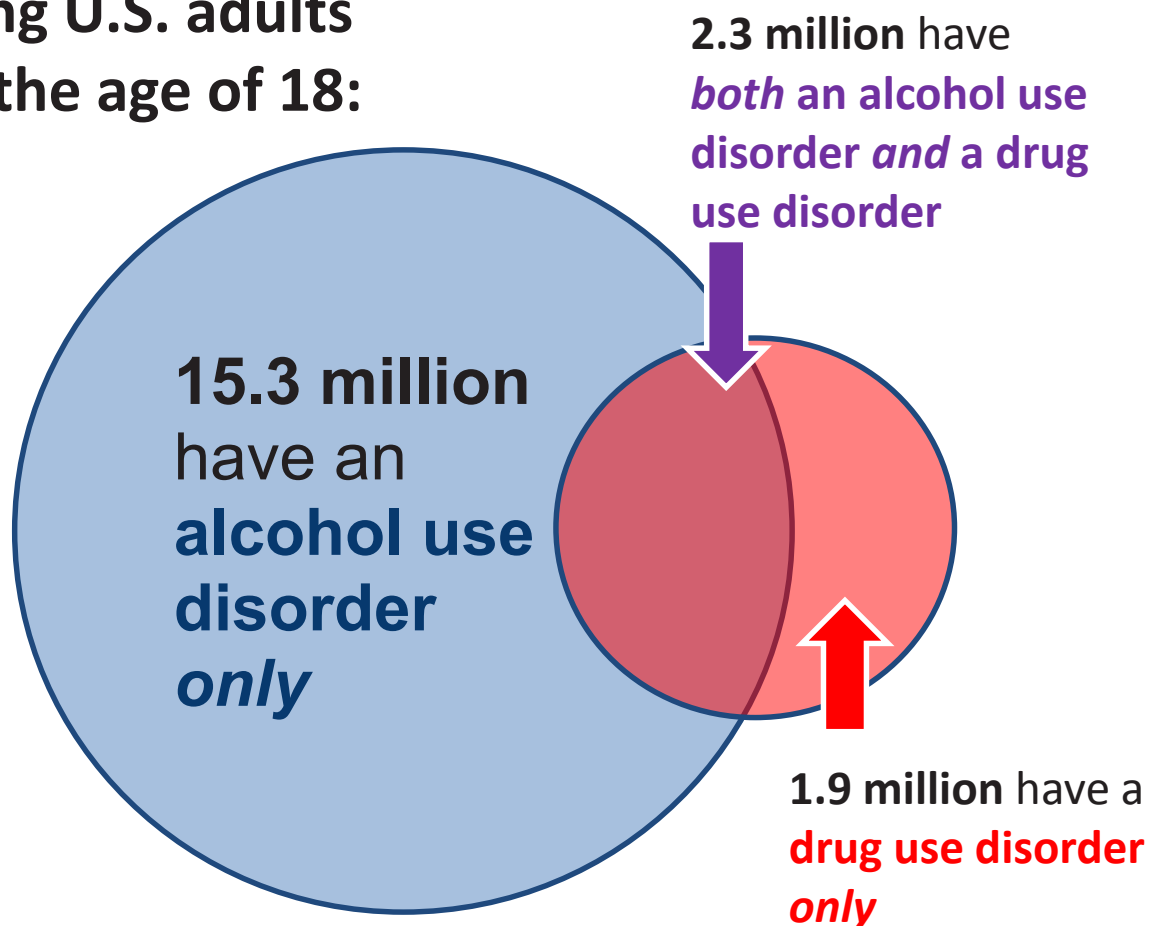
The article abstract can be found here: *Characterizing and reaching high-risk drinkers using audience segmentation.*

[http://www.ncbi.nlm.nih.gov/pubmed/19413650?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_DefaultReportPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/pubmed/19413650?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum)



# Alcohol Use Disorders Surpass Drug Use Disorders

**Among U.S. adults  
over the age of 18:**

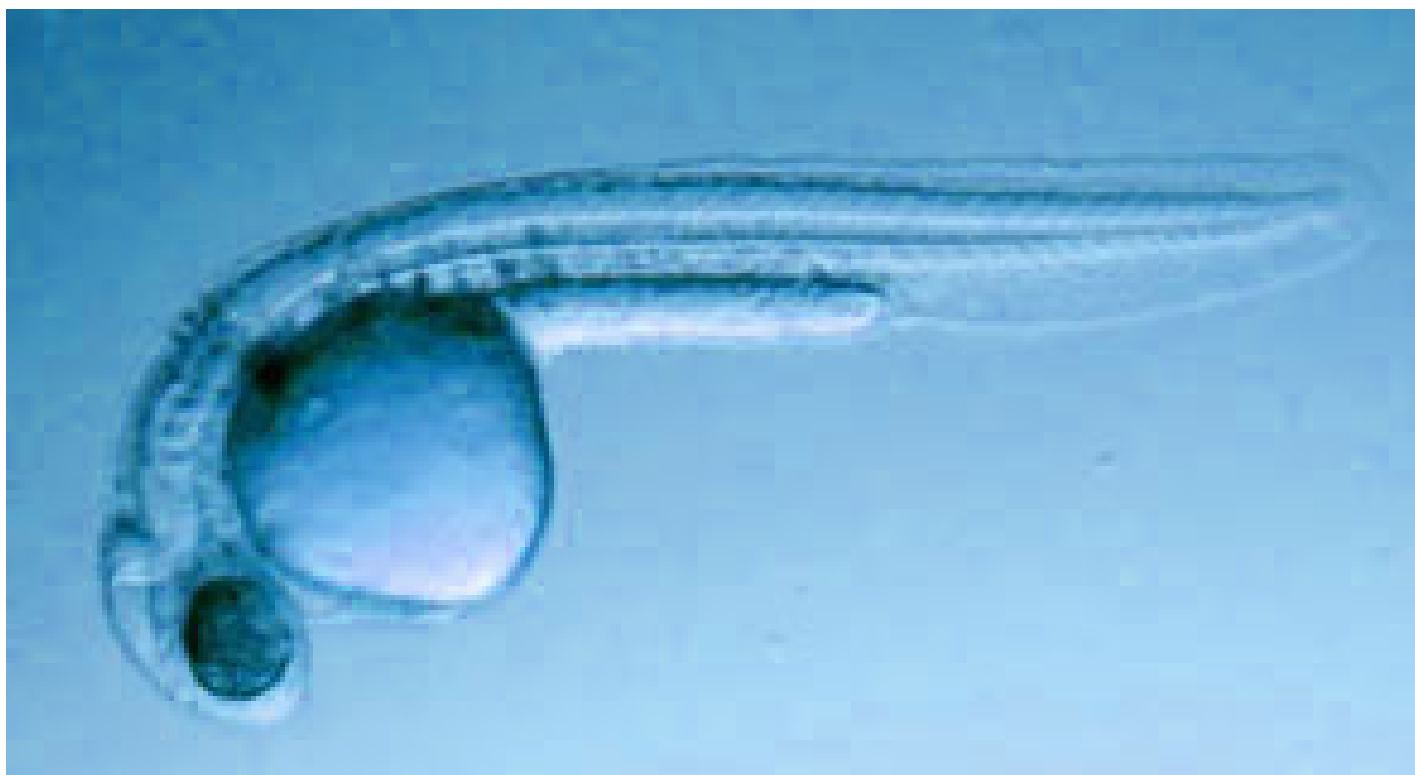


Millions more Americans have alcohol use disorders (abuse or dependence) than have drug use disorders. Most people who have alcohol use disorders do not have drug use disorders, but more than half of people with drug use disorders also have an alcohol use disorder. Nearly 80

percent of people with cocaine or hallucinogen disorders, for example, also have an alcohol use disorder; in contrast, among those with alcohol use disorders, fewer than 4 percent have a cocaine or hallucinogen use disorder. These and many other findings from NIAAA's National

Epidemiologic Survey on Alcohol and Related Conditions (NESARC) help to increase our understanding of how alcohol and drug use disorders occur in the population and can be used to improve prevention and intervention strategies. ■

# How Can a See-Through Fish Help Advance Alcohol Research?



Here's lookin' through you—zebrafish embryos allow researchers to observe organ development in live animals.

Why are zebrafish becoming an increasingly popular research model for exploring alcohol's effects on biology and behavior? For one thing, they have transparent embryos and even a see-through adult strain that allow researchers to observe the development and function of organ systems in live animals. Additionally, zebrafish have hundreds of offspring that

mature within a few months and are relatively inexpensive to keep. And importantly, zebrafish share a remarkable number of characteristics with humans, including extensive overlap in the genetic code; comparable early development processes; and similar biochemical pathways in the brain, liver, and other organs. Moreover, when exposed to alcohol, zebrafish show changes

in locomotion, aggression, and socialization that mimic behavior changes in humans. NIAAA intramural scientists and grantees are making use of this versatile animal model to discover connections between alcohol exposure and changes in gene function, embryonic development, liver metabolism, nerve cell function and activity, and behavior. ■



Dr. Bridget Grant

## 5 Questions With... Bridget Grant

**B**ridget Grant, Ph.D., Ph.D., is the Chief of NIAAA's Laboratory of Epidemiology and Biometry at NIAAA. She has directed all national NIAAA surveys since 1988 and most recently the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) since 2001.

### **In just a few sentences how would you describe the NESARC project?**

NESARC is a large survey of the U.S. adult population addressing all aspects of alcohol use. It includes a long list of questions addressing present and past alcohol consumption, alcohol use disorders, and use of alcohol treatment services. It is also the largest and most ambitious comorbidity study ever conducted, with questions related to tobacco and illicit drug use as well as psychiatric disorders associated with alcohol use disorders.

### **What are the advantages of having such a large survey size?**

The unprecedented sample size of NESARC ( $n = 43,093$ ) makes it possible to achieve stable estimates of even rare

conditions. Its oversampling of Blacks, Hispanics, and youth, and the inclusion of Hawaii and Alaska residents, provide enough minority respondents to make it an ideal vehicle for addressing the critical issue of race and ethnic disparities in disease prevalence, comorbidity, and access to health care services. NESARC is also a longitudinal survey with its first wave conducted in 2001–2002 and the second wave conducted in 2004–2005. The 70.9 percent overall response rate is excellent.

### **Who typically uses the NESARC database and what are they looking for?**

NESARC's data have several practical uses. It can help us understand high-risk drinking patterns, design better-targeted treatments, and monitor recovery

from alcohol use disorders in the general population.

NESARC's data can also track trends in the prevalence of alcohol use disorders over time; help define the relationship between alcohol use disorders and drug use, mood and anxiety disorders, and personality disorders; and illustrate the trends associated with driving after drinking.

### **Moving forward, are there any new ways that you would you like to see NESARC used—either by different types of researchers or for different purposes than currently?**

Analyses with NESARC data, especially Wave 1 in combination with Wave 2, have only just begun. As more researchers take advantage of the richness of this data set, more knowledge

will be gained. That will help identify risk factors and advance treatment interventions in the alcohol field.

In particular, in addition to the opportunities already discussed, I would hope that researchers will use NESARC to:

- Estimate the size, characteristics, and changing nature of special populations, including individuals with alcohol use disorders and others who are affected by the use of alcohol;
- Estimate changes in alcohol use disorders and their associated disabilities over time, and identify factors associated with the natural history of such disorders; and
- Determine the number of individuals receiving alcohol treatment through various programs and services, including those not otherwise represented in surveys of treatment facilities, as well as measuring the unmet need for alcohol treatment services and identifying barriers to seeking treatment.

**Your background is in epidemiology, statistics, and survey research in alcohol. If you were not an alcohol researcher, what other career might you have pursued?**

I would have pursued a veterinary medicine surgical specialty or aspired to be a Justice on the U.S. Supreme Court. ■■

## ABOUT US

*NIAAA Spectrum* is NIAAA's first-ever webzine. With engaging feature articles, short news updates, and colorful graphics, *NIAAA Spectrum* offers accessible and relevant information on NIAAA and the alcohol research field for a wide range of audiences. Each issue includes feature-length stories, news updates from the field, charticles and photo essays, and an interview with an NIAAA staff member or alcohol researcher. *NIAAA Spectrum* is published three times a year.

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